Jan H.J. Hoeijmakers

Jan Hoeijmakers started the molecular analysis of DNA repair in mammals at the Dept. of Genetics (Erasmus Univ. Rotterdam) in 1981. He cloned the first and subsequently many other human DNA repair genes, allowing elucidation of DNA repair mechanisms and of the basis of human repair syndromes, such as the cancer-prone xeroderma pigmentosum disorder and the severe neurodevelopmental conditions Cockayne syndrome and trichothiodystrophy. His team pioneered DNA repair dynamics in living cells exploring novel imaging technologies, generated numerous mouse repair mutants, discovered a strong connection between accumulation of DNA damage and (accelerated) aging and a trade-off between cancer and aging. The mouse mutants appeared superior models for Alzheimer’s disease addressing a tremendous unmet medical need. Accumulation of unrepaired DNA damage causing premature cell death and senescence also triggered an anti-aging ‘survival response’ which enhances maintenance at the expense of growth resembling the longevity response by dietary restriction. Remarkably, subjecting repair-deficient progeroid mice to actual dietary restriction tripled(!) their lifespan, drastically retarding DNA damage accumulation and accelerated aging most impressively neurodegeneration. These findings open perspectives for preventive interventions for healthy aging, reducing cancer and many aging-related diseases including neurodegeneration, and for therapy of human genome instability syndromes. For his work Jan Hoeijmakers received many prizes and awards.